

Figure 1a

```
1  CGCGTGGGCG CGTGCAGGAA CCCGGAGCAG CCGCGCACGG ACCACAGATG
51 CGCGCGGGCTG CCGCCTGCGC TCGCAGCTGG TGCCGGTGAG TGCCTCGGC
101 CTAGGCCACA GCTCCGACGA GCTGATACGT TTCCGCTTCT GCAGCGGCTC
151 GTGCCGTCGA GCACGCTCCC AGCACGATCT CAGTCTGGCC AGCCTACTGG
201 GCGCTGGGGC CCTACGGTCG CCTCCCGGGT CCCGGNCGAT CAGCCAGCCC
251 TGCTGCCGGC CCACTCGCTA TGAGGCCGTC TCCTTCATGG ACGTGAACAG
301 CACCTGNAGG ACCGTGGACC ACCTCTCCGC CACTGCCTGC GGCTGTCTGG
351 GCTGAGGATG ATCTATCTCC AAGCCTTT
```

Figure 1b

```
smcb2-00011-d2-a      29      59      89
                        AWAAGTRSSRARTTDARGCRLRSQLVVPS
                        :: ||| | ||| : || | ||| | |||
SW:NRTN_MOUSE      RLAQYRALQAGAPDAVELRELSPWAAARI PGPRRRAGPRRRAR-PGARPCGLRELEVRVS
                        60      70      80      90      100      110

smcb2-00011-d2-a      119      149      179      209      239      269
                        ALGLGHSSDELIRFRFCGSCRRARSQHDLSLASLLGAGALRSPPGSRPISQPCCRPTRY
                        ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : |||
SW:NRTN_MOUSE      ELGLGYTSDETVLFYRCAGACEAAIRTYDLGLRRLRQRRVRR---ERARAHPCCRPTAY
                        120      130      140      150      160

smcb2-00011-d2-a      299      329      359
                        E-AVSFMDVNSTWRTVDHLSATACGCLG*G*SISKP
                        | ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : |||
SW:NRTN_MOUSE      EDEVSFLDVHSRYHTLQELSARECACV*
                        170      180      190
```

Figure 1c

```
1  CGGACGCGTG GCGGACGCG TGGGCGCGTG CAGGAACCCG GAGCAGCCGC
51  GCACGGACCA CAGATGCGCG CGGCTGCCGC CTGCGCTCGC AGCTGGTGCC
101 GGTGAGTGCG CTCGGCCTAG GCCACAGCTC CGACGAGCTG ATACGTTTCC
151 GCTTCTGCAG CGGCTCGTGC CGCCGAGCAC GCTCCCAGCA CGATCTCAGT
201 CTGGCCAGCC TACTGGGCGC TGGGGCCCTA CGGTGCGCTC CCGGGTCCCG
251 GCCGATCAGC CAGCCCTGCT GCCGGCCAC TCGCTATGAG GCCGTCTCCT
301 TCATGGACGT GAACAGCACC TGGAGGACCG TGGACCACCT CTCCGCCACT
351 GCCTGCGGCT GTCTGGGCTG AGGATGATCT ATCTCCAAGC CTTTGACAC
401 TAGACCCATG TGTTGCCCTA CCTGGAACAG CTCCACCGGG CCTCACTAAC
451 CAGGAGCCTC AACTCAGCAG GATATGGAGG CTGCAGAGCT CAGGCCCCAG
501 GCCGGTGAGT GACAGACGTC GTCGGCATGA CAGACAGAGT GAAAGATGTC
551 GGAACCACTG ACCAACAGTC CCAAGTTGTT CATGGATCAC AGCTCTACAG
601 ACAGGAGAAA CCTCAGCTAA AGAGAACTCC TCTGGGAGAA TCCAGAAATG
651 GCCCTCTGTC CTGGGGAATG AATTTTGAAG AGATATATAT ACATATATAC
701 ATTGTAGTCG CGTTGCTGGA CCAGCCTGTG CTGAAACCAG TCCCGTGTTT
751 ACTTGTTGAA GCCGAAGCCC TATTTATTAT TTCTAAATTA TTTATTTACT
801 TTGCTGGTTT GTCAGATCCT TTCCTGGACA TGGGGGATGG TAGAAGAAGC
851 TAGATGAAGA TGTGCCCCAC CCCACCCCC CATCCACATT TTACACTTGA
901 CTCAGTAGTG CTACCTGGAT CGCCTACTTC TTGCCCCGCA GGTGTCTCTG
951 AGATGGATGG GAGGCACACA TAGGTGACAA AGATGCACAA TCCACAGTAC
1001 TTGGGGCCTG GGGTACCTAT GGGAAATAAA CAATATAGTT TTCTATGGAA
1051 AAAA
```

Figure 2

```
1   CCAAGCTTGG TACCGAGCTC GGATCCACTA GTAACGGCCG CCAGTGTGCT
51  GGAATTCGCC CTTACTCACT ATAGGGCTCG AGCGGCCGCC CGGGCAGGTA
101 TAAAAAAAAA AAGCGGCCTA GAATTCAGCG GCCGCTGAAT TCTAGGCTGC
151 CGCAGGAAGA GGGTGGGGAA ACGGGTCCAC GAAGGCTTCT GATGGGAGCT
201 TCTGGAGCCG AAAGCTATGG AACTGGGACT TGCAGAGCCT ACTGCATTGT
251 CCCACTGCCT CCGGCCTAGG TGGCAGTCAG CCTGGTGGCC AACCCTAGCT
301 GTTCTAGCCC TGCTGAGCTG CGTCACAGAA GCTTCCCTGG ACCCAATGTC
351 CCGCAGCCCC GCCGCTCGCG ACGGTCCCTC ACCGGTCTTG GCGCCCCCA
401 CGGACCACCT GCCTGGGGGA CACACTGCGC ATTTGTGCAG CGAAAGAACC
451 CTGCGACCCC CGCCTCAGTC TCCTCAGCCC GCACCCCCGC CGCCTGGTCC
501 CGCGCTCCAG TCTCCTCCCG CTGCGCTCCG CGGGGCACGC GCGGCGCGTG
551 CAGGAACCCG GAGCAGCCGC GCACGGACCA CAGATGCGCG CGGCTGCCGC
601 CTGCGCTCGC AGCTGGTGCC GGTGAGCGCG CTCGGCCTAG GCCACAGCTC
651 CGACGAGCTG ATACGTTTCC GCTTCTGCAG CGGCTCGTGC CGCCGAGCAC
701 GCTCCCAGCA CGATCTCAGT CTGGCCAGCC TACTGGGCGC TGGGGCCCTA
751 CGGTCGCCTC CCGGGTCCCG GCCGATCAGC CAGCCCTGCT GCCGGCCCAC
801 TCGCTATGAG GCCGTCTCCT TCATGGACGT GAACAGCACC TGGAGGACCG
851 TGGACCACCT CTCCGCCACT GCCTGCGGCT GTCTGGGCTG AGGATGATCT
901 ATCTCCAAGC CTTTGACAC TAGACCATG TGTTGCCCTA CCTGGAACAG
951 CTCCAAGGGC GAATTCTGCA GATATCCATC AACTGGCGG CCGCTCGAGC
1001 ATGCATCTAG AGG
```

Figure 3

1 MELGLAEPTA LSHCLRPRWQ SAWWPTLAVL ALLSCVTEAS LDPMSRSPAA
51 RDGPSPVLAP PTDHLPGGHT AHLCSERTLR PPPQSPQPAP PPPGPALQSP
101 PAALRGARAA RAGTRSSRAR TTDARGCRLR SQLVPVSALG LGHSSDELIR
151 FRFCSGSCRR ARSQHDLSLA SLLGAGALRS PPGSRPISQP CCRPTRYEAV
201 SFMDVNSTWR TVDHLSATAC GCLG*

Figure 4

Neurturin	10	20	30	40
Grnf4	10	20	30	40
Neurturin	50	60	70	80
Grnf4	50	60	70	80
Neurturin	100	110	120	130
Grnf4	100	110	120	130
Neurturin	140	150	160	170
Grnf4	140	150	160	170
Neurturin	180	190	200	210
Grnf4	180	190	200	210

Figure 5

ClustalW Formatted Alignments

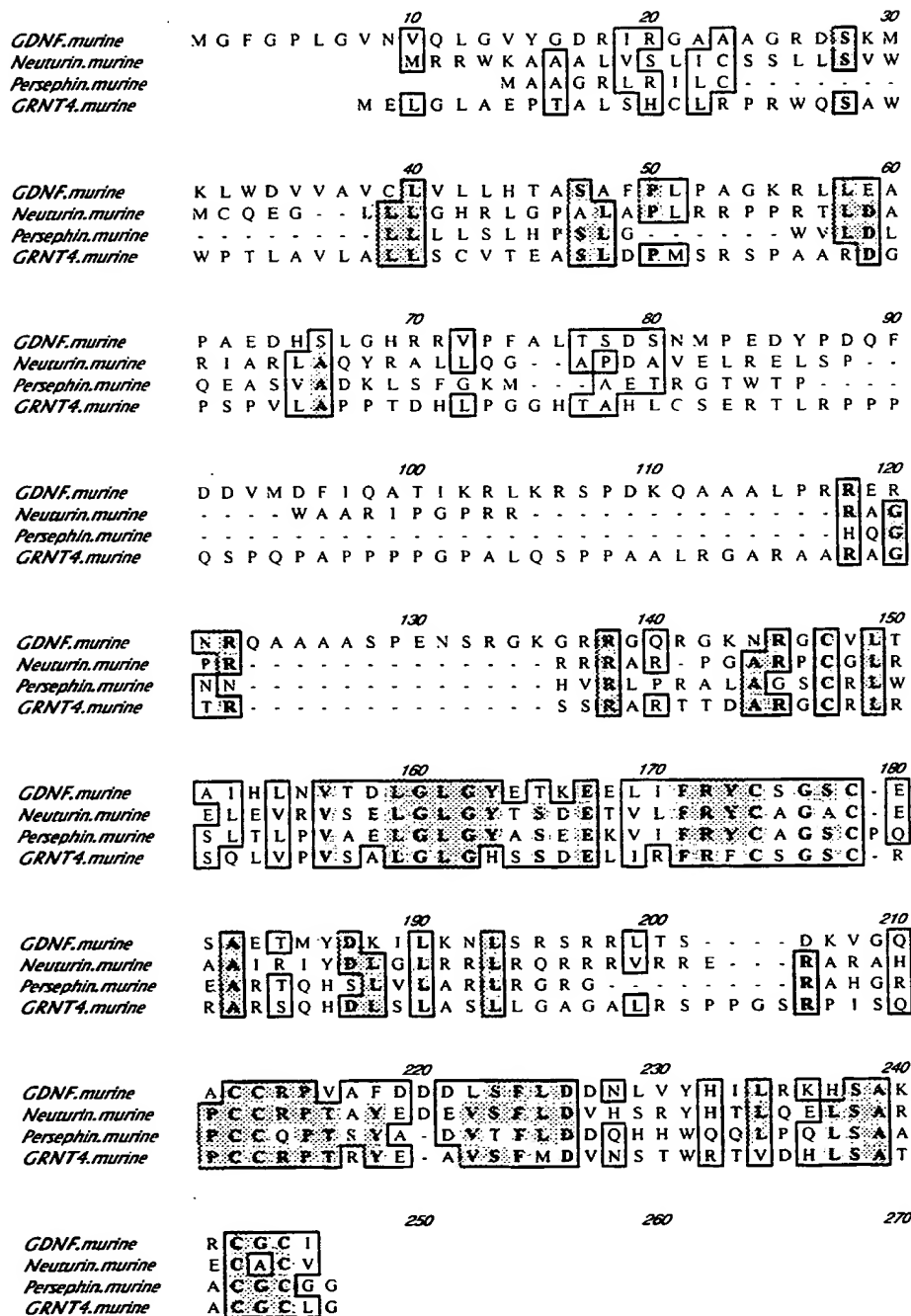


Figure 6

1 CAACAATGGC TGATGGGCGC TCCTGGTGTT GATAGAGATG GAACTTGGAC
51 TTGGAGGCCT CTCCACGCTG TCCCACTGCC CCTGGCCTAG GCGGCAGGCT
101 CCACTTGGTC TCTCCGCGCA GCCTGCCCTG TGGCCACCC TGGCCGCTCT
151 GGCTCTGCTG AGCAGCGTCG CAGAGGCCTC CCTGGGCTCC GCGCCCCGCA
201 GCCCTGCCCC CCGCGAAGGC CCCCCGCTG TCCTGGCGTC CCCC GCCGGC
251 CACCTGCCCG GGGGACGCAC GGCCCGCTGG TGCAGTGGAA GAGCCCGGCG
301 GCCGCCCGCG CAGCCTTCTC GGCCCGCGCC CCCGCCGCCT GCACCCCAT
351 CTGCTCTTCC CCGCGGGGGC CGCGCGGCGC GGGCTGGGGG CCCGGGCAGC
401 CGCGCTCGGG CAGCGGGGGC GCGGGGCTGC CGCCTGCGCT CGCAGCTGGT
451 GCCGGTGCGC GCGCTCGGCC TGGGCCACCG CTCCGACGAG CTGGTGCGTT
501 TCCGCTTCTG CAGCGGCTCC TGCCGCCGCG CGCGCTCTCC ACACGACCTC
551 AGCCTGGCCA GCCTACTGGG CGCCGGGGCC CTGCGACCGC CCCC GGGCTC
601 CCGGCCCCGTC AGCCAGCCCT GCTGCCGACC CACGCGCTAC GAAGCAGTCT
651 CCTTCATGGA CGTCAACAGC ACCTGGAGAA CCGTGGACCG CCTCTCCGCC
701 ACCGCCTGCG GCTGCCTGGG CTGAGGGCTC GCTCCA

Figure 7

1 MELGLGGLST LSHCPWPRRQ APLGLSAQPA LWPTLAALAL LSSVAEASLG
51 SAPRSPAPRE GPPPVLASPA GHLPGGRTAR WCSGRARRPP PQPSRPAPPP
101 PAPPSALPRG GRAARAGGPG SRARAAGARG CRLRSQLVVPV RALGLGHRSD
151 ELVRFRFCSG SCRRARSPHD LSLASLLGAG ALRPPPGSRP VSQPCCRPTTR
201 YEAVSFMDVN STWRTVDRLS ATACGCLG*

Figure 8

```

mouse      1 MELGLAEPTALSHCLRPRWQS.....AWWPTLAVLALLSCVTEASLD 42
           ||||| . ||||| |||. | ||||| ||||| |||||
human      1 MELGLGGLSTLSHCPWPRRQAPLGLSAQPALWPTLAALALLSSVAEASLG 50
           ||||| : ||||| ||||| ||||| ||||| |||||
mouse     43 PMSRSPAARDGPSFVLAPPTDHLPGGHTAHLCSERTLRPPPQSPQPAPPP 92
           ||||| : ||||| ||||| ||||| ||||| |||||
human     51 SAPRSPAPREGPPPVLASPAHLPGGRTARWCSGRARRPPPQPSRPAPPP 100
           ||||| : ||||| ||||| ||||| ||||| |||||
mouse     93 PGPALQSPPAALRGARAARAGTRSSRARTTDARGCRLRSQLVVPVSALGLG 142
           ||||| : ||||| ||||| ||||| ||||| |||||
human    101 PAP....PSALPRGGRAARAGGPGSRARAAGARGCRLRSQLVVPRALGLG 146
           ||||| : ||||| ||||| ||||| ||||| |||||
mouse    143 HSSDELIRFRFCGSCRRARSQHDLASLLGAGALRSPPGSRPISQPCC 192
           ||||| : ||||| ||||| ||||| ||||| |||||
human    147 HRSDELVRFRFCGSCRRARSPHDLASLLGAGALRPPPGSRPVSPQCC 196
           ||||| : ||||| ||||| ||||| ||||| |||||
mouse    193 RPTRYEAVSFMDVNSTWRTVDHLSATACGCLG* 225
           ||||| ||||| ||||| ||||| ||||| |||||
human    197 RPTRYEAVSFMDVNSTWRTVDRLSATACGCLG* 229
           ||||| ||||| ||||| ||||| ||||| |||||

```

Figure 9

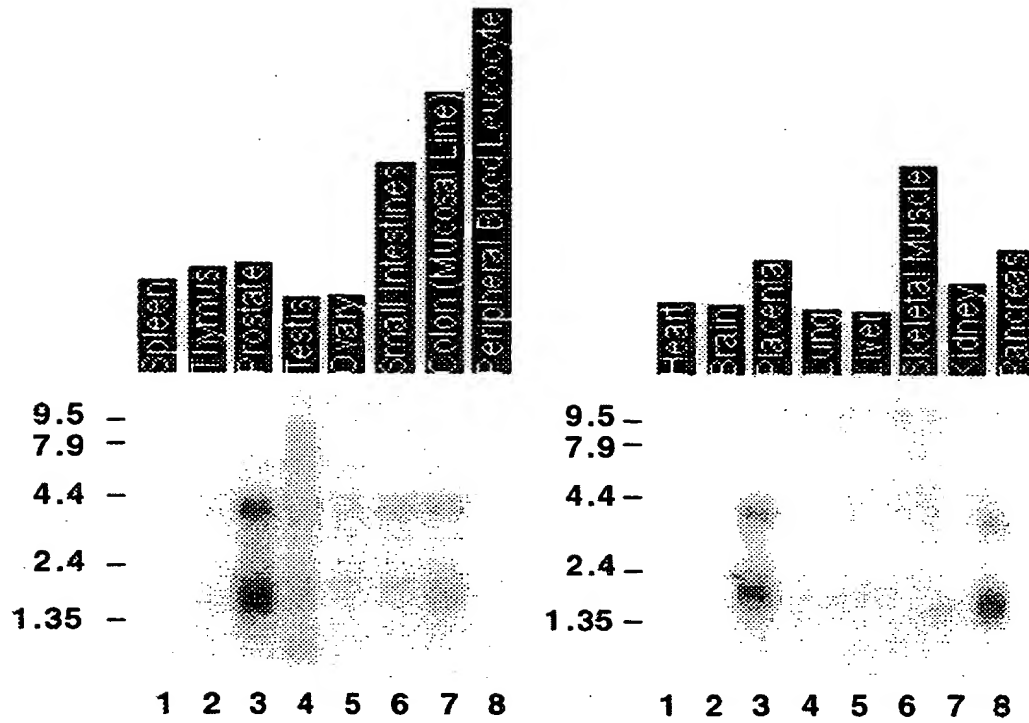


Figure 10

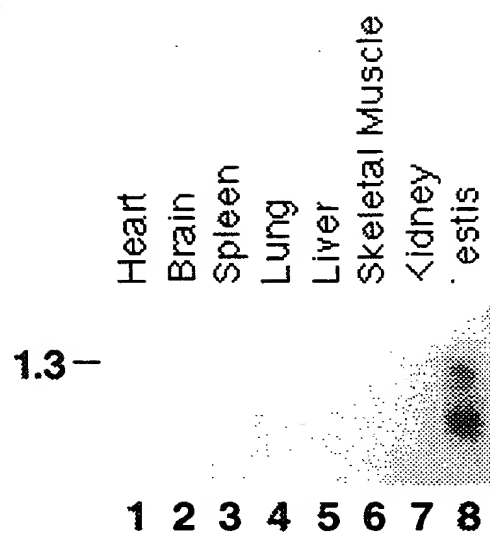


Figure 11



Figure 12

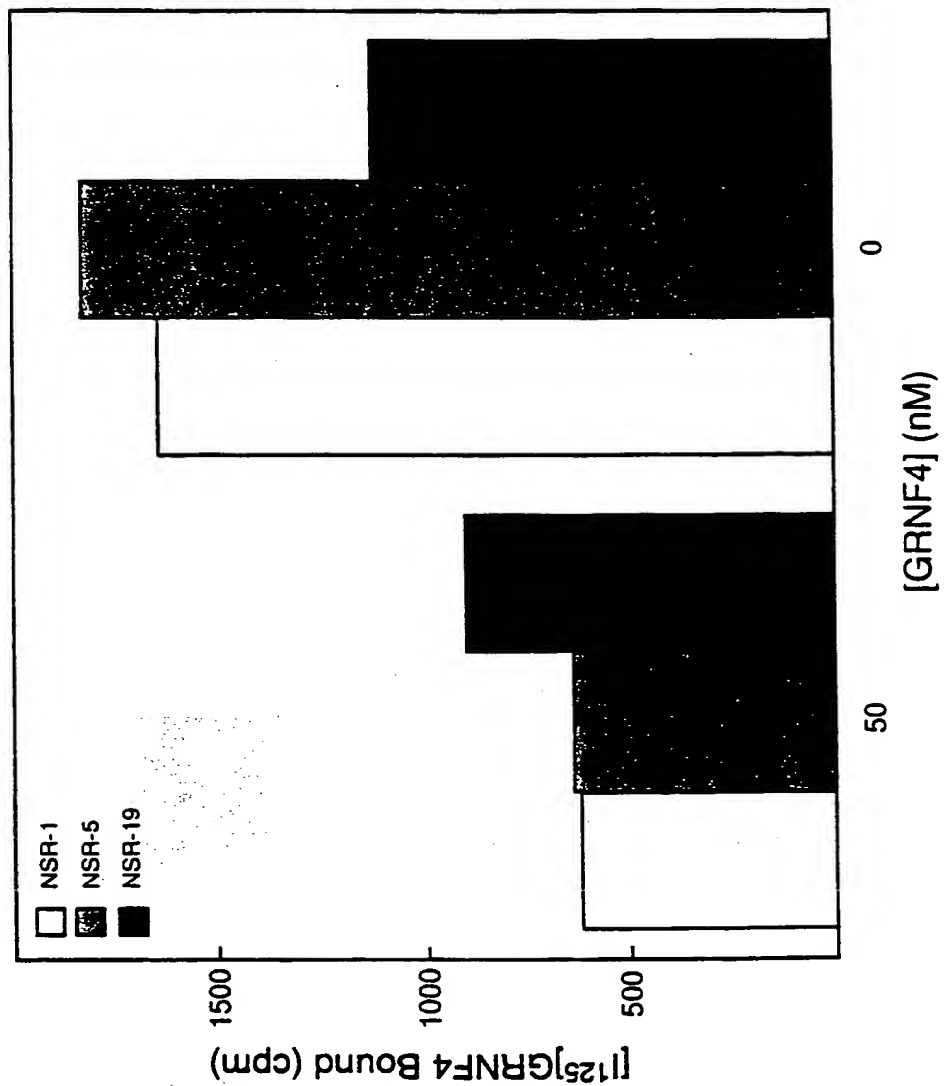


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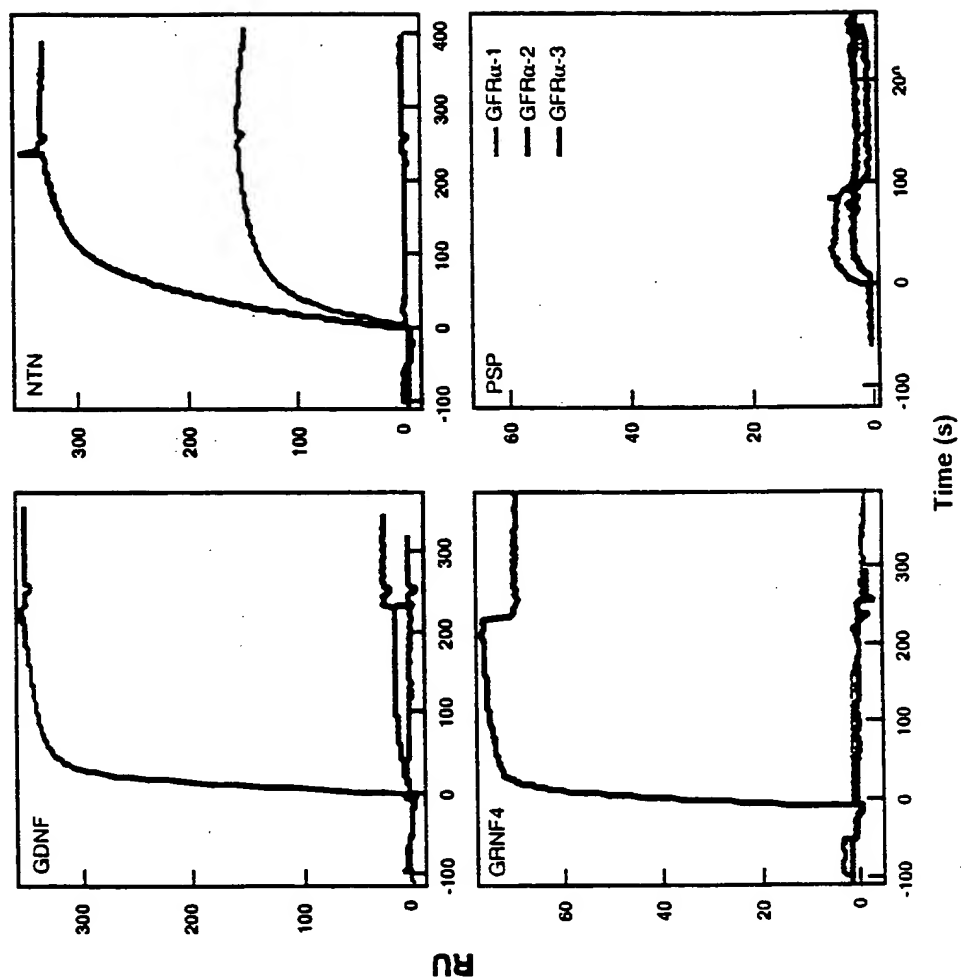


Figure 14

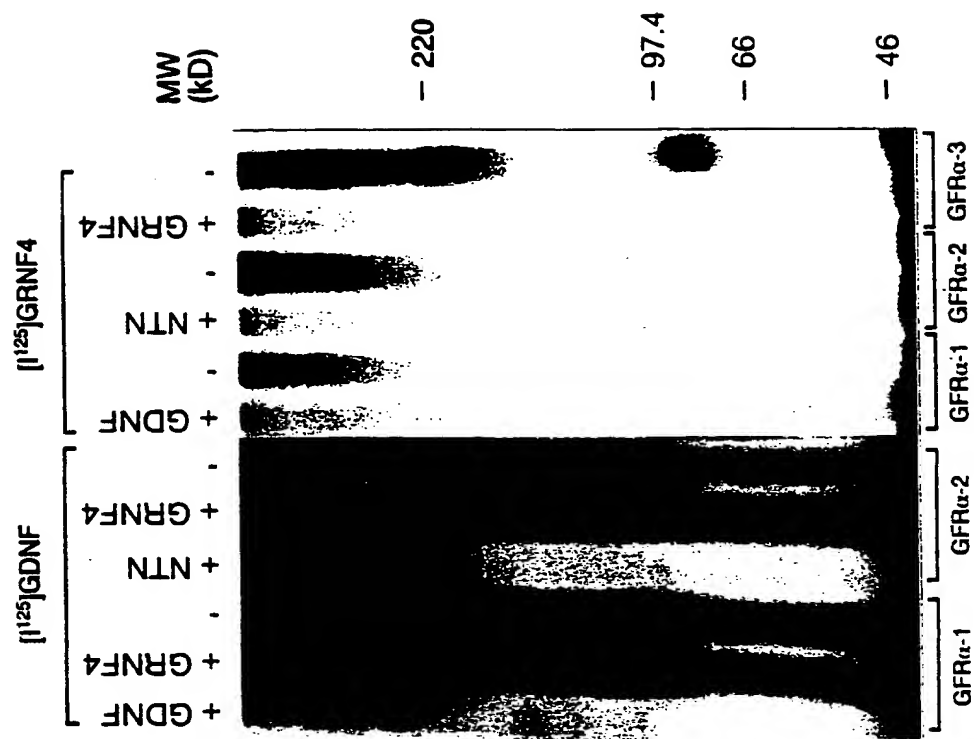


Figure 15

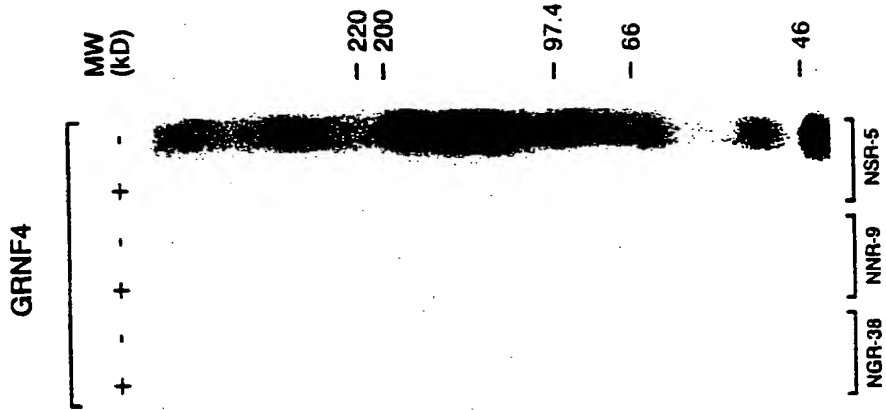


Figure 16

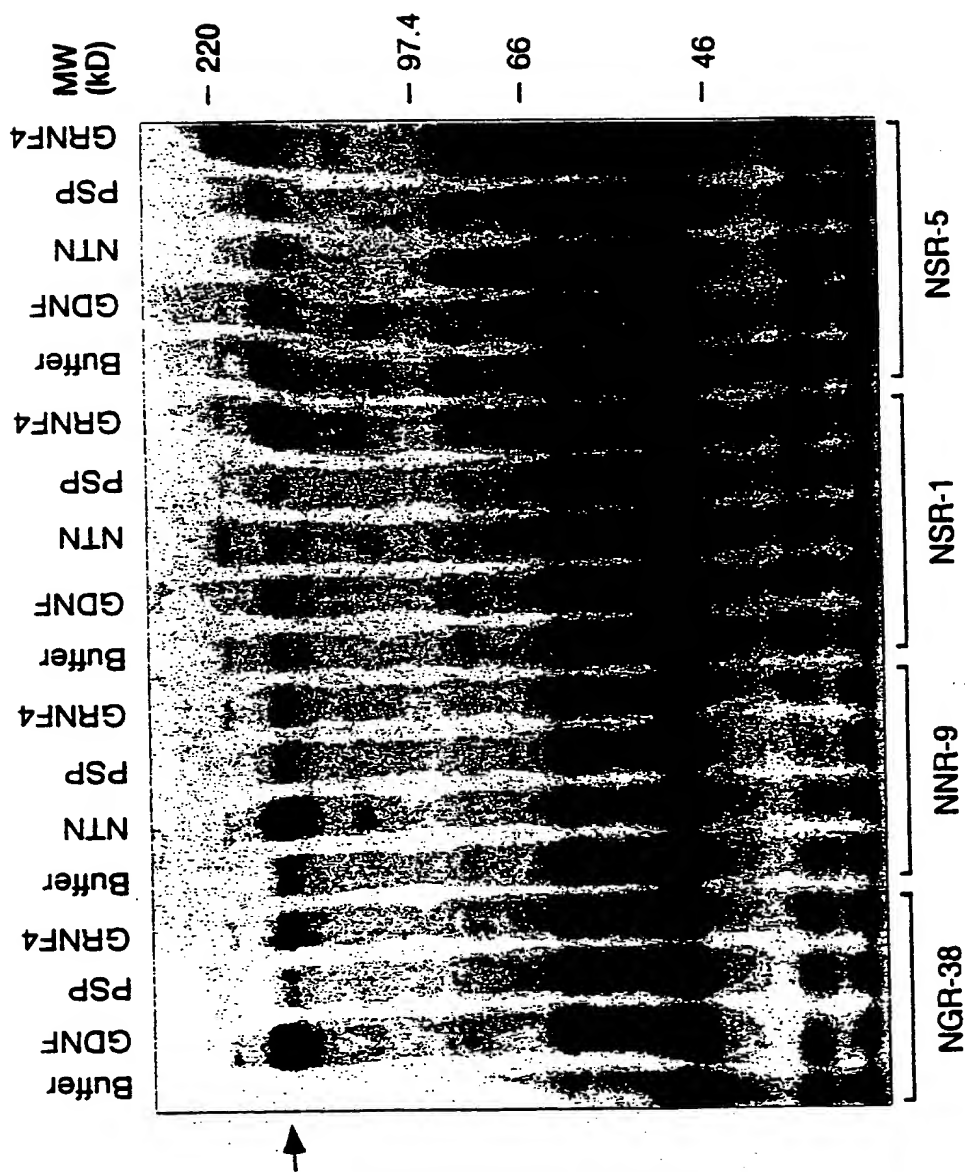


Figure 17

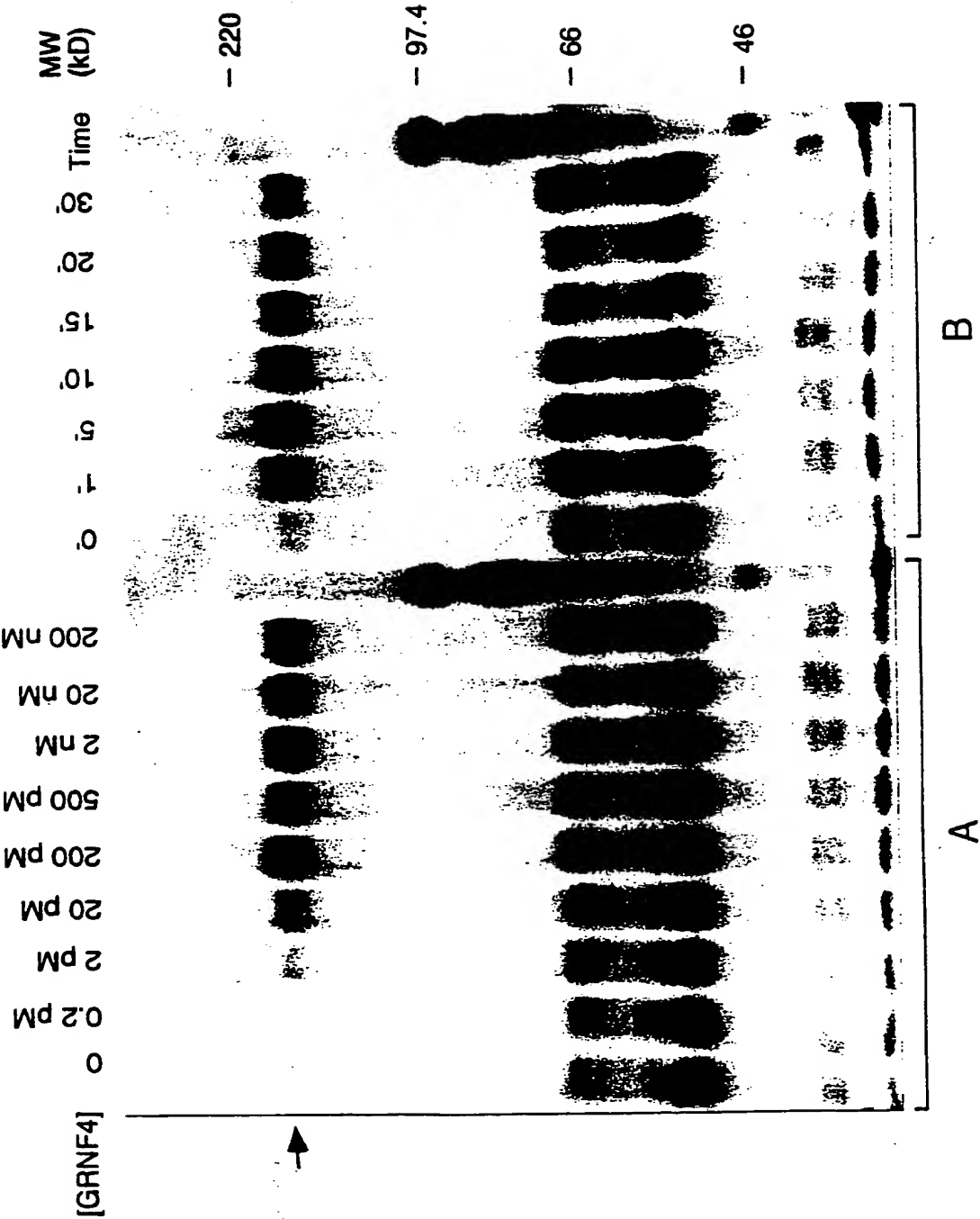


Figure 18

M E L G L (Xaa)₅ L S H C (Xaa)₂ P R (Xaa)_{0.4} (Xaa) Q (Xaa) A (Xaa) W P T L
A (Xaa) L A L L S (Xaa) V (Xaa) E A S L (Xaa)₄ R S P A (Xaa) R (Xaa) G P
(Xaa) P V L A (Xaa) P (Xaa)₂ H L P G G (Xaa) T A (Xaa)₂ C S (Xaa) R (Xaa)₂
R P P P Q (Xaa)₃ P A P P P P (Xaa) P (Xaa)₄ P (Xaa)_{0.4} R G (Xaa) R A A R A
G (Xaa)₃ S R A R (Xaa)₃ A R G C R L R S Q L V P V (Xaa) A L G L G H (Xaa)
S D E L (Xaa) R F R F C S G S C R R A R S (Xaa) H D L S L A S L L G A G A
L R (Xaa) P P G S R P (Xaa) S Q P C C R P T R Y E A V S F M D V N S T W R
T V D (Xaa) L S A T A C G C L G

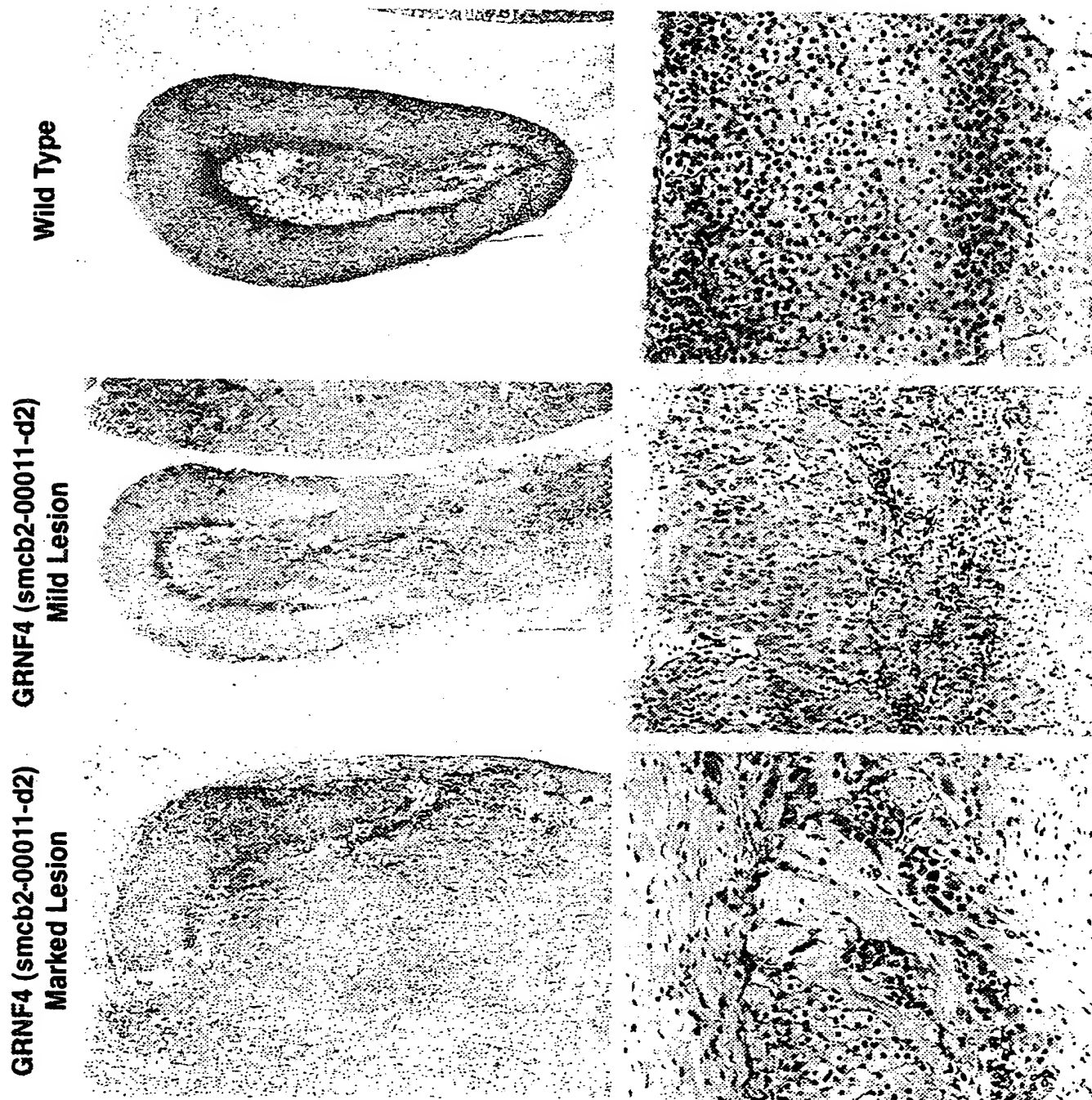
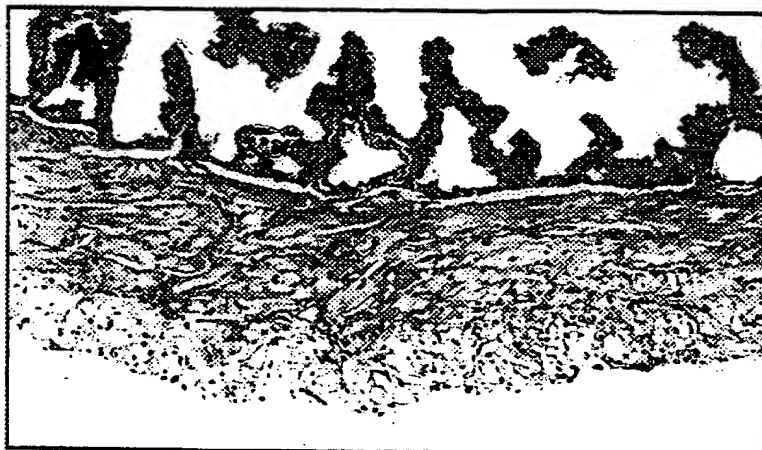
Figure 19

Figure 20

Wild Type



smcb2-00011-d2

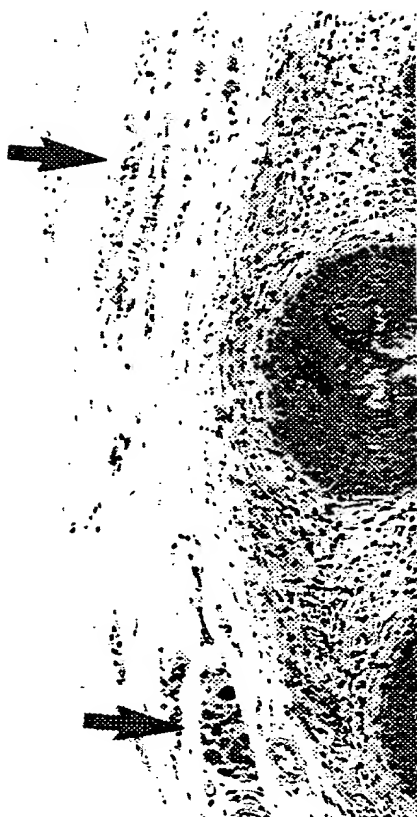


smcb2-00011-d2



Figure 21

Wild Type



smcb2-00011-d2

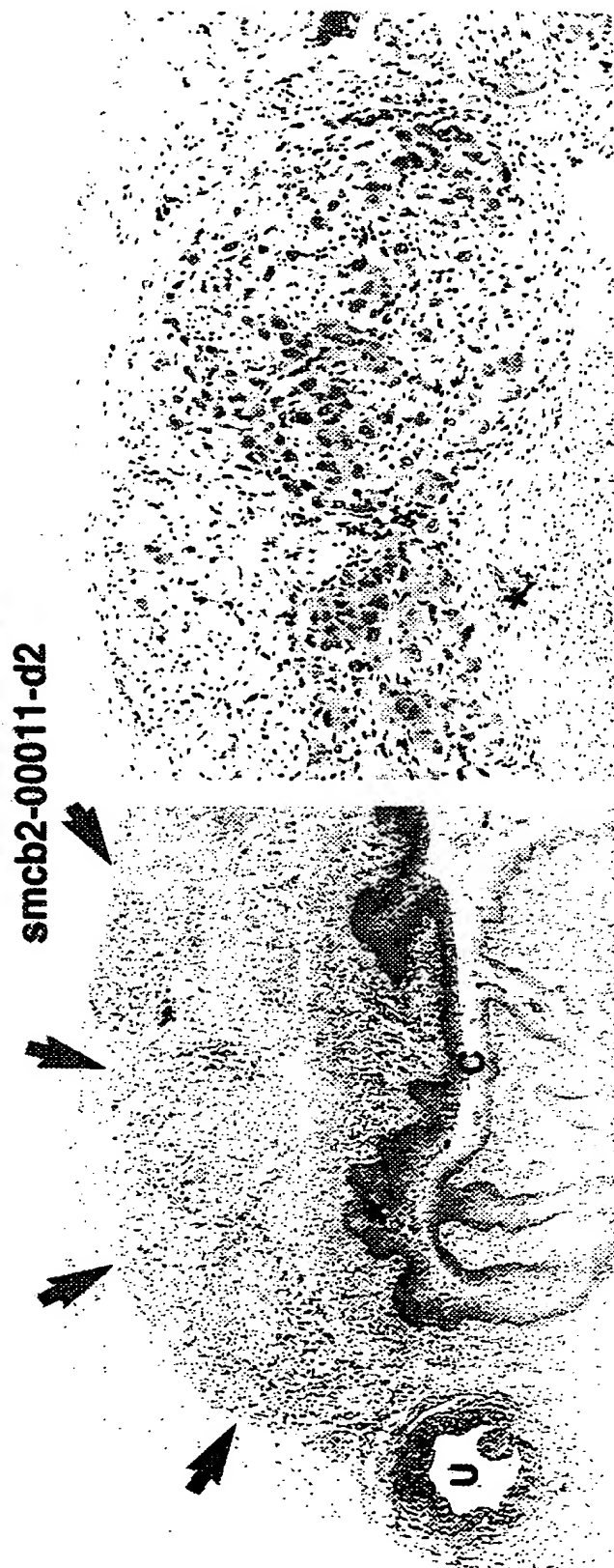
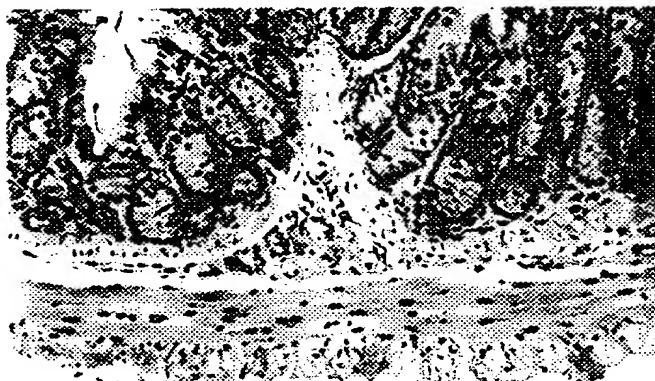


Figure 22**Wild Type****smcb2-00011-d2**